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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/728,055	12/04/2003	George Mulligan	MPI02-202P1RNM	8930

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EXAMINER	
REDDIG, PETER J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 05/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/728,055	MULLIGAN ET AL.	
	Examiner	Art Unit	
	Peter J. Reddig	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-28 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-28 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 21-24, drawn to a marker set comprising ONE isolated nucleic acid molecule from Tables 1, 2, or 3, classified in class 536, subclass 23.1.

(Upon election of Group I, applicant must further choose ONE nucleic acid molecule from Tables 1, 2, or 3, as each nucleic acid molecule represents an independent invention, not a species)

II. Claims 1, 2, 4-10, 25, and 26, drawn to a method for determining a proteasome inhibition therapy regimen for treating a tumor using ONE predictive marker wherein the level of expression of the marker is determined by detection of mRNA wherein the proteasome inhibition-based regimen for treating the tumor comprises treatment with bortezomib, classified in class 435, subclass 6.

(Upon election of Group I, applicant must further choose ONE polynucleotide predictive marker from Tables 1, 2, 3, 4, 5, or 6 as each polynucleotide molecule represents an independent invention, not a species)

III. Claims 1, 3-10, 25, and 27, drawn to a method for determining a proteasome inhibition therapy regimen for treating a tumor using ONE predictive marker wherein the level of expression of the marker is determined by detection of protein wherein the proteasome inhibition-based regimen for treating the tumor comprises treatment with bortezomib, classified in class 435, subclass 7.1.

(Upon election of Group I, applicant must further choose ONE polypeptide predictive marker from Tables 1, 2, 3, 4, 5, or 6 as each polypeptide molecule represents an independent invention, not a species)

IV. Claims 11, 12, 14-20, 25, and 26, drawn to a method for treating a tumor in a patient with a proteasome inhibition therapy by using ONE predictive marker wherein the level of expression of the marker is determined by detection of mRNA wherein the proteasome inhibition-based regimen for treating the tumor comprises treatment with a proteasome inhibitor selected from the group consisting of a peptidyl aldehyde, a peptidyl boronic acid, a peptidyl boronic ester, a vinyl sulfone, an epoxyketone, and a lactacystin analog, classified in class 514, subclass 2.

(Upon election of Group I, applicant must further choose ONE polynucleotide predictive marker from Tables 1, 2, 3, 4, 5, or 6 as each polynucleotide molecule represents an independent invention, not a species)

V. Claims 11, 13-20, 25, and 27, drawn to a method for treating a tumor in a patient with a proteasome inhibition therapy by using ONE predictive marker wherein the level of expression of the marker is determined by detection of protein wherein the proteasome inhibition-based regimen for treating the tumor comprises treatment with a proteasome inhibitor selected from the group consisting of a peptidyl aldehyde, a peptidyl boronic acid, a peptidyl boronic ester, a vinyl sulfone, an epoxyketone, and a lactacystin analog, classified in class 514, subclass 2.

(Upon election of Group I, applicant must further choose ONE polypeptide predictive marker from Tables 1, 2, 3, 4, 5, or 6 as each polypeptide molecule represents an independent invention, not a species)

VI. Claim 28, drawn to a method for identifying a candidate compound for treatment of cancer, classified in class 435, subclass 7.1.

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claim 23 has been renumbered 25.

Misnumbered claim 24 has been renumbered 26.

Misnumbered claim 25 has been renumbered 27.

Misnumbered claim 26 has been renumbered 28.

The inventions are distinct, each from the other because of the following reasons:

The invention of Group I and the methods of Groups II-V are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (I) the process for using the product as claimed can be practiced with another materially different product or (ii) the product as claimed can be used in a materially different process of using that product [see *MPEP* § **806.05(h)**]. In the instant case the antibody product as claimed can be used in a materially different process such as a probe in a nucleic acid hybridization assay like Southern analysis.

Furthermore, searching all of the claims (i.e., Groups I and Groups II-V) would invoke a burdensome search because the inventions have been classified separately. Thus, each invention has attained recognition in the art as a separate subject for inventive effort, and also a separate

field of search. This would necessitate different searches in the patent and or non-patent literature and the consideration of different patentability issues.

Inventions of Group I and Group VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the invention of Group I is a product that is comprised of nucleic acid molecules while Group VI is a method that employs the structurally distinct polypeptide molecules.

Searching all of the claims (i.e., Group I and Group VI) would invoke a burdensome search, as described above, because the inventions have been classified separately.

Inventions of Group II and IV and Groups III and V are directed to related methods. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j).

In the instant case, the methods of Group II and IV and Groups III and V are related in that they are broadly drawn to methods involving a proteasome inhibition therapy regimen using a predictive marker. The groups are distinct in that Groups II and IV employ the materially distinct step of determining the level of the predicative marker by detection of mRNA. This step is not employed in Groups III and V. The methods of Groups III and V are directed to polypeptide detection.

As described, searching all of the claims (i.e., Groups II and IV and Groups III and V) would invoke a burdensome search, because the inventions have been classified separately.

Furthermore, searching the inventions of Group II and IV and Groups III and V together would impose a serious search burden. In the instant case, the search of the polypeptides and polynucleotides are not coextensive. In cases such as this one where descriptive sequence information is provided, the sequences are searched in appropriate database. There is search burden also in the non-patent literature. Prior to the concomitant isolation and expression of the sequences of interest there may be journal articles devoted solely to polypeptides, which would not have described the polynucleotide. Similarly, there may have been "classical" genetics papers, which had no knowledge of the polypeptide but spoke to the gene. Searching, therefore is not coextensive. In addition, the claims include a multitude of distinct sequences inclusive of various complements and fragments. This search requires an extensive analysis of the art retrieved in a sequence search and will require an in-depth analysis of technical literature. As such, it would be burdensome to search the inventions of Group II and IV and Groups III and V.

Inventions of Group II and Group IV are directed to related methods. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j).

In the instant case, Group II and IV are related in that they are broadly drawn to methods involving a proteasome inhibition therapy regimen using a predictive marker wherein the level of expression of the marker is determined by detection of mRNA. The groups are distinct in that Group II employs the materially distinct step of using bortezomib for the proteasome inhibition-based regimen while Group IV employs a proteasome inhibitor selected from the group

consisting of a peptidyl aldehyde, a peptidyl boronic acid, a peptidyl boronic ester, a vinyl sulfone, an epoxyketone, and a lactacystin analog.

Furthermore, searching all of the claims of Groups II and IV would invoke a burdensome search because the inventions have been classified separately. Thus, each invention has attained recognition in the art as a separate subject for inventive effort, and also a separate field of search. This would necessitate different searches in the patent and or non-patent literature and the consideration of different patentability issues.

Inventions of Group III and Group V are directed to related methods. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j).

In the instant case, Group III and V are related in that they are broadly drawn to methods involving a proteasome inhibition therapy regimen using a predictive marker wherein the level of expression of the marker is determined by detection of protein. The groups are distinct in that Group II employs the materially distinct step of using bortezomib for the proteasome inhibition-based regimen while Group IV employs a proteasome inhibitor selected from the group consisting of a peptidyl aldehyde, a peptidyl boronic acid, a peptidyl boronic ester, a vinyl sulfone, an epoxyketone, and a lactacystin analog.

Furthermore, searching all of the claims of Groups III and V would invoke a burdensome search because the inventions have been classified separately. Thus, each invention has attained recognition in the art as a separate subject for inventive effort, and also a separate field of search.

This would necessitate different searches in the patent and or non-patent literature and the consideration of different patentability issues.

Inventions of Groups II-V and Group VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06).

In the instant case, the different inventions are unrelated in that the inventions of Groups II-V are broadly drawn to a method for treating a tumor with a proteasome inhibition therapy regimen. Group VI is drawn to a method for identification of a compound for treatment of cancer. The identification of a compound is unrelated to methods of therapy in that it does not require the use of patients and the medical facilities required for the testing of therapies. Additionally, the binding assay of Group VI is not required for the methods of Groups II-V.

Furthermore, searching all of the inventions of Groups II-VI would invoke a burdensome search. Some of the inventions have been classified separately. Thus, each of these inventions has attained recognition in the art as a separate subject for inventive effort, and also a separate field of search. Although some of the inventions are classified similarly, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not coextensive and is much more important in evaluating the burden of search.

Because these inventions are distinct for the reasons given above and the search required for one group is not required for another group, restriction for examination purposes as indicated is proper.

Species Elections for Groups II-V

Claims 7 and 17 of Groups II-V are generic to the following disclosed patentably distinct species for "liquid tumor":

1) myelomas

2) multiple myloma

3) Non-Hodgkins Lympoma

4) B-cell lymphoma

5) Waldenstrom's syndrome

6) chronic lymphocytic leukemia

7) other leukemias

Claim 19 of Groups IV and V are generic to the following disclosed patentably distinct species of "proteasome inhibitor":

1) peptidyl aldehyde

2) peptidyl boronic acid

3) peptidyl boronic ester

4) vinyl sulfone

5) epoxyketone

6) lactacystin analog

Claims 27of Groups III and V are generic to the following disclosed patentably distinct species of "detection reagent":

1) an antibody and its derivative or fragment

2) peptide probe

In accordance with the decisions in *In re Harnisch*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984), restriction of a Markush group is proper where the compounds within the group either (1) do not share a common utility, or (2) do not share a substantial structural feature disclosed as being essential to that utility. In addition, a Markush group may encompass a plurality of independent and distinct inventions where two or more members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the other member(s) obvious under 35 USC 103.

The above species are independent or distinct because they comprise structurally distinct molecules and have different modes of operation and different effects. Further, each species would require different searches and the consideration of different patentability issues.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an

allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Note:

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Applicant is advised that the reply to this restriction requirement to be complete must include an election of the invention to be examined even though the requirement is traversed (37 CFR 1.143).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER

Peter J. Reddig, Ph.D.
Examiner
Art Unit 1642

PJR